UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/184,572	11/02/1998	LISA MCKERRACHER	99999/MARUSY	4396

7590 08/27/2002

WILLIAM J HONE
FISH & RICHARDSON
SUITE 2800
45 ROCKEFELLER PLAZA
NEW YORK, NY 10111

EXAMINER
TURNER, SHARON L

ART UNIT	PAPER NUMBER
1647	24

DATE MAILED: 08/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/184,572	McKerracher et al
Examiner	**Art Unit**
Sharon L. Turner	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 16, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *25-29, 32, and 33* is/are pending in the application.

4a) Of the above, claim(s) *25-29* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *32 and 33* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *25-29, 32, and 33* are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Nov 2, 1998* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-16-02 has been entered.

2. Claims 25-29 and 32-33 are pending.

3. Claims 25-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

4. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Priority

5. Receipt of the priority document is acknowledged. However, it is noted that the data presented in the priority document and the specification as filed 11-2-98 differ substantially. In particular the disclosure of the priority document is limited to C3 transferase mediated suppression of the inhibition of axon outgrowth in PC12 cells in vitro, whereas the specification of the application exemplifies C3 transferase mediated suppression of the inhibition of axon outgrowth in crushed optic nerve, an in vivo exemplification. Claims 32-33 are drawn to a method wherein the effects and delivering are required to be at a CNS or PNS lesion site in a

patient. As the PC12 in vitro data is not an art accepted model for prediction of in vivo neuronal axonal out growth, see for example Crutcher et al., CRC Crit. Rev. in Neurobiol., 2(3):297-33, 1986, p. 298, lines 17-18 which teach that the relevance of the data from PC12 cells to normal neuronal growth is not clear, the effective filing date awarded instant claims is that of the '572 application filing date, 11-02-1998.

Specification

6. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

7. The disclosure is objected to because of the following informalities: The figure legends require reference to the appropriate views where the views are referenced in the figures.

Appropriate correction is required.

Drawings

8. The drawings are objected to under 37 CFR 1.83(a) because they fail to show the views as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

It is noted that applicants drawings reflect views where views are not referenced in the figure legends and similarly the specification discusses views where no views appear to be noted.

Appropriate correction which is consistent is required.

Claim Objections

9. Claim 33 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 33 is improperly dependent on claim 33. The typographical error should be corrected such that claim 33 is dependent on claim 32. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The examiner recognizes various ADP-ribosyl transferases in particular mouse, human, chicken, *C. difficile*, however the examiner does not recognize ADP-ribosyl transferase C3 from other than *C. botulinum*. Thus, it appears that claim 33 does not further limit claim 32 and in contrast broadens the scope of claim 32 to ADP-ribosyl transferases from species other than *C. botulinum*.

Applicants argue that their claim amendments of 1-16-02 obviate the rejection.

Applicant's arguments filed 1-16-02 have been fully considered but are not persuasive. The claim amendments are directed to a process wherein the process requires a particular product and the product as claimed is recited by a product by process limitation. However, the MPEP stipulates that a product by process limitation does not distinguish the product, see in particular 2113 and 2173.05. Therefore the product by process limitation is not deemed to further limit the parent claim or to provide a suitable Markush group as only *C. botulinum* ADP-ribosyl transferase is recognized in the art and the process limitation does not distinguish the product from the protein already recited. Thus, the objection is maintained as of record.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 32-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

The specification discloses ADP-ribosyl transferase C3 enzyme from *C. botulinum.* However, claim 32 recites a recombinant ADP-ribosyl transferase generically which recitation encompasses and corresponds to various polypeptide structures from other species, which are not described in the specification as originally filed or recognized in the art. Thus, no generic family of these compounds is disclosed or recognized and therefore the generic recitation fails to meets the written description provision of 35 USC 112, first paragraph. The artisan can not immediately recognize alternative species of the generic molecules encompassed by the claims. In addition, as the examiner cannot find support for the use of such alternative recombinant species in the claimed method, the generic recitation is not supported by the application as filed and would constitute new matter. Applicant's should either point to the specification where written description support for the genus recitation of a recombinant ADP-ribosyl transferase may be found or amend the independent claim to be clearly drawn to *C. botulinum* ADP-ribosyl transferase C3 enzyme as recognized in the art.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 32-33 stand rejected under 35 U.S.C. 102(e) as being anticipated by Liao et al., US Patent No. 6,180,597 issued 1-30-01, filed 8-11-98.

Liao et al., teach a method of treating an individual for example for hypoxia or brain injury comprising administration of a compound which a rho GTPase function inhibitor in an amount effective to increase endothelial cell NOS activity in brain tissue. The specification discloses such inhibitors as compounds including C. botulinum ADP-ribosyl C3 transferase administered at for example 50 ug/ml, see in particular column 13, line 64-column 14, line 16, examples 1-26 and claims 1-93. The administration may be in vivo or in vitro as claimed. Liao teach administration via intravenous, subcutaneous, intramuscular routes or via infusion, see in

particular columns 15-17, especially, column 16, lines 48-61. The administration is for increasing blood flow and increasing ecNOS in tissues and thus necessarily involves exposure to the PNS throughout the body including at lesion sites which would necessarily result from ischemia. In particular, Liao teaches administration for a method of reducing brain injury resulting from stroke or ischemia and necessitates increasing the activity of ecNOS in brain tissue, see also claims 22, 86 and 90-91 and thus the administration necessarily results in the administration of C3 transferase to the CNS and the PNS at the site of ischemic lesions. Thus, the reference teachings anticipate the claimed invention absent evidence to the contrary because the property of suppressing said inhibition of neuronal axon outgrowth is inherently provided.

14. Claims 32-33 stand rejected under 35 U.S.C. 102(e) as being anticipated by Johnson et al., US Patent No. 5,851,786 issued 12-22-98, filed 9-27-95.

Johnson et al., teach a method of treating an individual to regulate actin polymerization, stress fiber formation and/or focal adhesion assembly by administration of a compound such as Botulinum C3 exoenzyme also known as ADP-ribosyl C3 transferase at 100ng/ul, see in particular column 14, line 56-line 15, line 59, column 18, lines 30-63 and Example 3, including administration directly to a cell in vivo, ex vivo or systemically, see in particular column 18, line 44. Additionally administration is as in column 15-16 including subcutaneous, intramuscular or transdermal. The administration may be measured functionally including detecting neuronal response and for a therapeutic composition for the treatment of Parkinson's or Alzheimer's disease, see in particular Abstract and column 17, lines 18-58 and claim 40. As the

administration routes are systemic the administration necessarily results in the administration at sites of lesion including to neurons within the PNS and CNS. It is further noted that the method is effective to treat Alzheimer's and Parkinson's disease which are recognized as affecting CNS brains neuronal cells which exhibit focal lesions. Thus, the reference teachings anticipate the claimed invention absent evidence to the contrary because the property of suppressing said inhibition of neuronal axon outgrowth is inherently provided.

Status of Claims

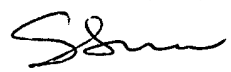
15. No claims are allowed.

Conclusion

16. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.



Sharon L. Turner, Ph.D.
August 26, 2002